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Supratherapeutic anti-factor Xa levels in patients receiving prophylactic doses of enoxaparin: A case series

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ABSTRACT

INTRODUCTION: Enoxaparin prophylaxis prevents venous thromboembolism in surgical patients. Real time anti-Factor Xa monitoring for surgical patients on enoxaparin prophylaxis is increasingly common.
PRESENTATION OF CASES: We report on three cancer patients with therapeutic or supratherapeutic anti-Factor Xa levels while on prophylactic doses of enoxaparin after surgical procedures. In all cases, elevated anti-Factor Xa levels were the result of blood specimens being removed from a heparinized chemoport.
DISCUSSION: This case series highlights the importance of peripheral venipuncture or appropriate blood wasting from central access sites for anti-Factor Xa levels.
CONCLUSION: Inappropriately drawn anti-Factor Xa levels may contribute to prophylaxis interruption or unnecessary workup for renal or liver failure.

1. Introduction

Cancer, presence of central venous access, and surgery are recognized risk factors for venous thromboembolism. Cancer patients who have extirpative surgery or reconstructive surgery are commonly prescribed enoxaparin, a low molecular weight heparin, for post-operative VTE prophylaxis [1,2]. Enoxaparin is typically prescribed as a fixed dose among the non-obese population, although emerging literature supports that patient level factors such as larger extent of surgical injury and higher gross weight identify patients who may metabolize enoxaparin more quickly [3,4]. Anti-Factor Xa (aFXa) level is a surrogate marker for enoxaparin effectiveness and safety. aFXa monitoring and individualized enoxaparin dosing is increasingly common for surgical patients who receive enoxaparin prophylaxis [3–6].

Many cancer patients have residual chemoports after neoadjuvant chemotherapy. Patients with poor peripheral venous access often have these ports accessed for routine medication and fluid administration after surgical procedures. In patients with poor quality veins, labs can also be drawn through the chemoport. Here, we report on three patients with reported therapeutic or supratherapeutic aFXa levels while on prophylactic doses of enoxaparin as a result of port-associated unfractionated heparin contamination.

We are presently enrolling surgical patients into prospective clinical trials for real time aFXa monitoring and pharmacist driven enoxaparin dose adjustment at the University of Utah (clinicaltrials.gov identifiers NCT02687204 and NCT02704052). Patients receive a standard dose of enoxaparin and have steady state peak and trough aFXa levels drawn at 4 and 12 h after the third dose, respectively. Goal peak aFXa levels for once and twice daily administration are 0.3–0.5 IU/mL and 0.2–0.4 IU/mL, respectively. Goal trough levels are 0.1–0.2 IU/mL for both once and twice daily dosing [7,8]. aFXa levels ≥0.5 IU/mL are considered to represent therapeutic anticoagulation [9]. Patients with out of range peak aFXa levels receive real time dose adjustment to optimize enoxaparin effectiveness and safety [3,4,6].

2. Presentation of cases

2.1. Case 1

A 45 year old woman with body mass index 31.6 kg/m^2 and a history of breast cancer had a four hour procedure for bilateral tissue expander to implant exchange and pedicled latissimus muscle flap to cover a radiated tissue expander site. She previously had neoadjuvant chemotherapy through a tunneled internal jugular vein chemoport. Subcutaneous enoxaparin 40 mg twice daily was

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initiated on post-operative day zero. Steady state peak and trough aFXa were 0.70 IU/mL and >2.00 IU/mL (the upper limit of the test), respectively. Enoxaparin was discontinued and her creatinine and liver function tests were demonstrated to be within normal limits. Twenty four hours after her last enoxaparin dose, aFXa level was still >2.00 IU/mL. Investigation revealed that the labs had been drawn from the chemoport instead of peripheral venipuncture. The port had been maintained with 100 units of heparin twice daily. aFXa level drawn via peripheral venipuncture at 36 h after last enoxaparin dose was undetectable, and the patient subsequently had an in range peak aFXa (0.26 IU/mL) on enoxaparin 30 mg twice daily.

2.2. Case 2

A 30 year old man with body mass index 20.1 kg/m^2 and a mediastinal germ cell tumor had a four hour procedure for en bloc resection of a mediastinal mass with a lung wedge resection. He previously had neoadjuvant chemotherapy through a tunneled subclavian vein chemoport. Enoxaparin 40 mg once daily was initiated on post-operative day one. His baseline creatinine, liver function tests, and coagulation parameters were all within normal limits. Steady state peak aFXa level was drawn via a peripheral venipuncture and was 0.58 IU/mL. Steady state trough aFXa level was reported at 1.26 IU/mL. Investigation revealed that his chemoport had been accessed on the day of lab draws and 500 units of heparin were administered twice daily for line maintenance. The second set of labs had been drawn from the heparinized chemoport. He was discharged prior to repeat labs.

2.3. Case 3

A 53 year old woman with a body mass index of 28.2 kg/m^2 and a history of breast cancer had a seven hour procedure for delayed right breast reconstruction with a unilateral deep inferior epigastric perforator free flap. She had received adjuvant chemotherapy through a left subclavian chemoport. During surgery, her chemoport was transiently accessed and was then heparinized (dose unknown) prior to the needle being removed. Enoxaparin 40 mg twice daily was initiated on post-operative day one. Steady state aFXa was drawn after the third enoxaparin dose through her previously heparinized chemoport and was 0.71 IU/mL. Steady state peak and trough aFXa drawn via peripheral venipuncture after her fourth dose were 0.42 IU/mL and 0.16 IU/mL, respectively. She subsequently had an in range peak aFXa (0.38 IU/mL) on enoxaparin 30 mg twice daily prior to discharge.

3. Discussion

Real time monitoring of enoxaparin effectiveness using aFXa level is increasingly common among surgical patients [3–6]. This manuscript provides several important learning points for surgeons who plan to monitor aFXa levels. Non-heparinized blood tubes are required for aFXa specimens to avoid specimen contamination and test invalidation [9]. aFXa levels drawn from heparinized central venous lines, peripherally inserted central catheters, or chemoports may be falsely elevated. These falsely elevated levels may contribute to unneeded workup for renal or liver failure and may also cause unnecessary interruption of enoxaparin prophylaxis. This is particularly relevant because prophylaxis interruption is associated with downstream VTE events [10]. aFXa levels are ideally drawn via peripheral venipuncture but can theoretically be drawn from central venous access if an appropriate volume of blood is wasted prior to lab collection.

4. Conclusion

Real time anti-Factor Xa levels are being increasingly used to optimize enoxaparin prophylaxis in surgery patients. This case series highlights the importance of appropriate collection of blood specimens to avoid heparin contamination and falsely elevated anti-Factor Xa levels.

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Conflict of interest

None of the authors has a financial interest in any of the products, devices, or drugs mentioned in this manuscript.

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Author contribution

Pannucci—Study design, data collection, writing, Varghese—Study design, writing, Graves—Study design, writing, Prazak—Data collections, data analysis, writing.

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Consent

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